REMARKS

Applicants appreciate the courtesy of the Examiners in discussing the claimed invention in an interview with Applicants' Attorney.

The specification has been amended to delete references to attorney docket numbers and replace them with references to application serial numbers. No new matter is presented by the amendments.

**Claim Rejections under 35 USC 103 should be withdrawn**

Claims 1-16, 18 & 20-24 are rejected under 35 USC 103(a) as allegedly being unpatentable over Urdea et al. (1989) in view of Lockhart et al. (2000). Applicants respectfully disagree with the Examiner and traverse this rejection of the claims.

Urdea et al discusses methods for detecting a single analyte using binding probes (B, figure 1) and label probes (A, figure 1). A target is bound by multiple probes in multiple regions (Figure 1). No methods for detecting multiple analytes are disclosed. As pointed out by the Examiner, no hybridization pattern is generated for detection. In contrast, Claims 1-16, 18 & 20-24 recite methods for detecting a plurality of targets and including a step of "detecting the nucleic acid targets based upon the hybridization pattern."

The Office Action alleges that one of skill in the art would be motivated to combine Urdea et al. with Lockhart et al. in order to detect multiplicity of genes in order to provide a high throughput analysis of multiple genes with high signal to noise ratio. Urdea et al. teaches that "traditional solid phase assay involves an extended period of time and requires careful washing to minimize non-specific background signals." (Col. 1, Lines21-24). "By

providing for annealing of nucleic acid sequences in solution, the time for performing the assay can be substantially diminished as compared to annealing on a solid surface and the number of separations and washing steps required can be limited and be less critical, so as to reduce technician error. Reagents containing complementary sequences can be added in excess during or at the end of the denaturation to inhibit renaturation of double stranded DNA and to react rapidly with the analyte strand by diffusion in solution. The rate of binding to the solid support can also be accelerated by the presence of a large amount of the binding pair member bound to the support. In addition, by adding the label conjugate as the last reagent, the analyte will be present in a highly concentrated form." (Col. 2., Lines 24-39).

Applicants respectfully submit that the discussion by Urdea et al does not provide any motivation or suggestions to use multiple probes in microarray assays. Rather, adding a large number of mediator probes would increase the complexity of microarray based assays. The primary advantage of the Claimed methods is the flexibility of the assay, i.e., one type of array can be used as a universal array to detect different sets of targets by using different mediator probes.

Because there is no motivation or suggestion in the cited references to combine the cited references, applicants respectfully submit that the Examiner has failed to establish a prima facie obviousness. Therefore, this rejection of Claims 1-6, 18 and 20-24 should be withdrawn.

Claims 17 and 19 are rejected under 35 USC 103(a) as allegedly being unpatentable over Urdea et al. in view of Lockhart et al and further in view of Vinayak et al. For the

above reasons, applicants respectfully submit that it is not prima facie obvious to use mediator and cipher probes to detect multiple analytes. Therefore, this rejection of Claims 17 and 19 should also be withdrawn.

For the foregoing reasons, Applicants believe all the pending claims are in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5699.

The Commissioner is authorized to charge any fees or credit any overpayments associated with this application to Deposit Account No. 01-0431.

Respectfully submitted,

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ATTACHMENT A

Marked up paragraph showing the changes in brackets and underlines that the accompanying submission makes to the specification of USSN 09/747,004.

In some embodiments, the cipher probes are at least 15, 20, 25, 30, 35, 40, 45 and 50 bases in length. In one probe selection method, all possible probes of given length is first generated. The probe sequences are compared with biological sequences in public and private databases. Probes that are complementary to known biological sequences are eliminated from the candidate probe pool. The remaining probes are selected for their hybridization characteristics. The selected cipher probes have similar hybridization characteristics and minimal homology to biological sequences. The hybridization characteristics may be selected based upon certain rules and/or based upon predicted hybridzation behavior of the probes. Methods for selecting optimal probes for gene expression are disclosed in for example, U.S. Patent Nos. 5,800,992, and 6,040,138, U.S. Patent Application Serial No. 60/252,617, [attorney docket number 3369,] and U.S. Patent Application Serial No. 60/252,617, [attorney docket number 3373,] all incorporated here by reference for all purposes.